Engineering Aspects of Herbal and Phytochemical Processing: A Malaysian Perspective

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ABSTRACT

Malaysia has a strong knowledge base of herbal product usage with a wide user base. Several Malaysian herbs have strong potential to be developed into global herbal medicines such as *Tongkat Ali* for impotence, *Kacip Fatimah* for hormone replacement therapy and *Hempedu Bumi* for diabetes and hypertension. In order to produce herbal medicines, standardisation, i.e. the process of producing herbal extracts or phytochemicals in which product potency is guaranteed through consistency in active compound profile and content level, is essential. Proper process development and effective analysis are the keys to standardisation.

Process development of herbal processing in Malaysia involves modelling and optimisation studies of extraction equipment such as batch solid liquid extraction. In order to build effective process models and apply process design methods, physical and chemical data is required of the local herbs. At present very little knowledge is available of such parameters such as solubility, partition coefficient and heat transfer coefficients.

In order to build a niche in the herbal medicine market, Malaysia can undertake product development based on local knowledge in terms of product formulation, form, and usage. Lastly, the experiences at the Chemical Engineering Pilot Plant (CEPP), the national research centre for process and product development in natural products and bioprocess is covered.

Keywords: Malaysian herbal industry, herbal and phytochemical processing, process development, product development

INTRODUCTION

Malaysia has a rich tradition of herbal product usage for food, health and beauty. With its 3 major races – Malay, Chinese and Indian, and a diverse indigenous community, there is a wealth of knowledge within the nation as well as a large user base of herbal products. In 1997, Malaysians consumed over RM 4.55 billion worth of herbal related products, of which over 80% was imported (Puteh, 1999), indicating an opportunity in herbal product processing.

In Malaysia, herbal products cannot be sold as medicines i.e. taken for a specific illness with a prescribed dosage unless a clinical trial has been carried out and the safety aspects as well as dosage related effects have been established as required by the Drug Control Authority (DCA). However, herbs based on traditional knowledge can be sold provided the manufacturer does not make any medicinal claims and that the product passes safety tests. This is a route that several pharmaceutical as well as herbal companies have taken with regards to marketing products within Malaysia. The DCA does however require that the manufacturing process be GMP compliant.

The objective of this paper is to give an overview of the engineering aspects of herbal and phytochemical production in Malaysian. Emphasis is given in the area of herbal production, standardisation and analysis, process and product development and the experiences at the Chemical Engineering Pilot Plant (CEPP).

MALAYSIAN HERBAL PRODUCTION

Herbal products in Malaysia are sold in a variety of forms – raw material, infusions and decoctions, herbal extracts, essential oils, creams and oils. The herbal production process runs from planting to value added production as outlined in Table 1 where each stage involves some level of engineering.

There are several major herbs being developed as herbal products in Malaysia for both the local and international market including Tongkat Ali, Kacip Fatimah, and Hempedu Bumi. These herbs are highly effective for current global illnesses and health concerns and are of interest to develop into herbal medicines. A brief overview of these herbs is given below.

Tongkat Ali, *Eurycoma longifolia* (Figure 1a), is a traditional Malay and indigenous herb used as an aphrodisiac, general tonic, anti-Malarial, and anti-pyretic remedy. Scientifically it has also been found to have anti-tumour and anti oxidant properties and has been biochemically shown to increase testosterone production as well as to overcome impotence.

Kacip Fatimah, *Labisia pumila* (Figure 1b), is a herb used in the treatment of post partum mothers, gonorrhoea, rheumatism, pile, and bone diseases. It is currently undergoing clinical trials for its estrogenic and androgenic properties to develop an effective herbal medicine for hormone replacement therapy or estrogen related therapy.

Table 1: Engineering aspects of herbal production

STAGE	ENGINEERING CONTRIBUTION
Planting and harvesting	Sensors and monitoring, harvesting equipment
Preprocessing	Grinding, drying and storage, quality tests
Processing	Extraction method, on-line sensors, chemical analysis, optimisation, process synthesis and design, new extraction methods, batch process optimisation
Value added and final product production	Spray or freeze drying, mixing and formulation, batch processing, product engineering, final form production – capsule, tablets.

Hempedu Bumi, *Andrographis paniculata* (Figure 1c), is used for anti-pyretic, anti-fertility, treatment of appetite loss, anti-diabetes, anti-hypertensive, and skin condition – eruption and scabies. Malaysian researchers are studying its anti-diabetic and anti-hypertensive properties.

STANDARDISATION AND ANALYSIS

Herbal efficacy is determined by the specific profile and content of the complex mixture of phytochemicals within the herb. Various factors such as location, planting conditions and processing affect the final profile of herbal extracts. It is therefore critical to maintain the herbal extract efficacy level through standardisation. Standardisation is the process of producing herbal extracts or phytochemicals in which product potency is guaranteed through consistency in active compound content level. Presently there are two standardised extracts produced in Malaysia by Nova Laboratories for Tongkat Ali and Hempedu Bumi (Novalab, 2004). This process requires high knowledge in phytochemical analysis and process technology to ensure the quality assurance required.

Several analysis methods are utilised to determine the quality of herbal material and products. Chemical analysis through UV-Vis, HPLC, and LC-MS are applied to determine the phytochemical content of herbal extracts. However, these methods are limited to identified compounds only as listed in Table 2 and require independent chemical standards for confirmation. A key disadvantage of these methods is the slow testing time as well as the high cost of equipment. For small to medium sized enterprises, a more cost effective and faster alternative to chemical testing is desirable.

Alternatively, electronic nose and taste technology has been applied to herbal products in raw or processed form. This involves both sensor technology as well as pattern matching methods such as multivariate analysis and Artificial Intelligence. Work is currently being done in Malaysia on the development of these sensors at Universiti Sains Malaysia (Abdul Rahman *et al.*, 2004). An advantage of this method is that the qualitative properties of the herbal material in either raw or processed form can be compared against the profile of the pure herb without knowledge of the chemical components. This method allows for easy determination of herb origin, quality as well as purity.

(a) Tongkat Ali (b) Kacip Fatimah (c) Hempedu Bumi

Figure 1: Major herbs in Malaysia

PROCESS DEVELOPMENT

Once a herbal extract, bioactive fraction, or purified phytochemical has been identified as a viable product, it becomes an engineering task to turn the small scale lab product into a large scale speciality chemical manufacturing process.

Predominantly there are three key steps in phytochemical processing, i.e. a solid-liquid extraction (leaching) process, a purification process and a final product production step. Phytochemicals are usually extracted from plant raw material using water or food grade alcohol in a batch solid-liquid extraction process or a percolating process. In the purification step, downstream separation processes such as liquid extraction, evaporation, membrane filtration, chromatographic separation, and adsorption are used to obtain a concentrated extract that contains the desired phytochemicals. Lastly, the extract is turned into powder form via freeze drying or spray drying. An example of phytochemical processing is Tongkat Ali extract production as shown in Figure 2. This phytochemical processing that was developed in CEPP involves water extraction, filtration and spray drying to produce a high quality spray dried Tongkat Ali extract powder.

From an engineering point of view, there are two specific challenges in herbal and phytochemical processing. Firstly, to increase product yield while maintaining overall process reasonable economics and secondly, to produce a standardised extract with the active ingredients available in the desired concentration and profile.

Standardised extracts have a fixed phytochemical profile such as those outlined for Ginseng G115 and Ginkgo Biloba EGb761 in Table 3. Apart from the appropriate planting and preprocessing required, the most important step in standardisation is the extraction process. The selection of the appropriate extraction process as well as the determination of the optimum process parameters is crucial in producing standardised extracts. Studies need to be done into the effects of processing parameters such as processing duration, extraction temperature, solvent to raw material ratio, and particle size of raw material on phytochemical yield and profile.

Table 2: Chemical markers and family for Malaysian herbs

Plant	Marker	Chemical Family
TONGKAT ALI	eurycomanone	quassinoid
PEGAGA	asiaticoside	triterpenoid saponin
HEMPEDU BUMI	andrographolide	diterpene lactone

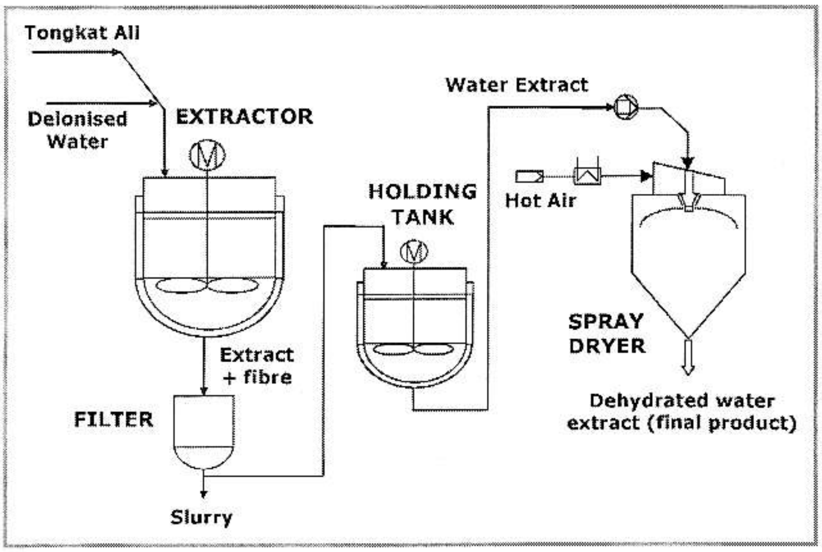

Figure 2: Tongkat Ali water extract production process

Table 3: Standardised extracts of Ginseng and Ginkgo Biloba

EXTRACT	GINKGO EGb761 (DE FEUNDIS, 1998)	GINSENG G115 (SOLDATI, 1998)
Process	Patented Process (1972)	Trade Secret
Owner	Schwabe, Germany	Pharmaton SA, Switzerland
Process	18 step extraction process Acetone – water extract	Ethanol-water extract
Qualitative measures	< Negligible ginkgolic acids < 20-30 % flavonoid glycosides < 2.5-4.5% ginkgolides A,B, C & J	< 4% ginsenosides (saponins) < 100 mg extract is equivalent to 500 mg raw material

A common problem in phytochemical processing is the lack of important process data. In contrast to the well-established petrochemical and palm oil-based oleochemical industries in Malaysia, much of the critical data for phytochemical processing is still currently unknown. Among the critical information needed for processing include physical and chemical data such as:

- Density and molecular weight of plant material and extract powder
- Diffusion, partition, and mass transfers coefficients for separation processes
- Heat transfer properties of the extract and plant material, e.g. heat capacity, heat transfer coefficient, etc.
- Liquid extract properties, e.g. viscosity, solubility parameters, Henry coefficient, etc.

Studies on Tongkat Ali extraction have determined the effects of particle size and solvent ratio on yield (Kaur *et al.*, 2003), the partition coefficients, solid diffusivity and overall mass transfer coefficients (Sim *et al*, 2004) as well as the optimal number of extraction stages (Sahar, 2004). In addition, batch optimisation studies on Tongkat Ali water extract production has also been carried out, which resulted in new flowsheet designs with higher throughput and better returns on investment (Athimulan *et al*, 2004).

In addition to process optimisation, the effects of processing on the biological activity of the herbal extract need to be investigated as has been done on tumeric (*curcuma longa*), a herb with high anti-oxidant activity. It was found that antioxidant activity was not necessarily increased when the yield of the oleoresin which contained the active ingredients was increased by adjusting the extraction solvent mixture (Hashim, 1999).

An illustrative example of process engineering can be shown based on the process outlined in the patent application for a bioactive protein enriched fraction of Tongkat Ali, which is claimed to have aphrodisiac effects (Sambandan et al, 2004). In the patent application, a laboratory scale extraction and purification method was developed to produce this fraction as shown in Figure 3.

Several questions to be addressed from a process engineering point of view to produce a standardised extract of this fraction on a larger scale such as:

- At what stage of the extraction does the main protein fraction leach out?
- Can other solvents target the required fraction better?
- Does the raw material particle size affect the protein fraction leaching?
- What is the stability of the protein fraction?
- Can the chromatographic stage be replaced by any other separation process such as membrane separation?
- Is the freeze drying process necessary as the required chromatographic concentration can be achieved through an evaporator or an enhanced extraction process?

A new process may be developed to produce the equivalent protein enriched fraction possibly with only two main unit operations, extraction and purification. The extraction process may be either a batch solid liquid extraction or percolative extraction while the purification may be a membrane filter or chromatographic method such as size exclusion and displacement chromatography. Another alternative may a process intensification step similar to the membrane bioreactor utilised in bioprocess engineering where separation is combined with extraction. To systematically design an optimum process flowsheet for phytochemical processing, a recently developed hierarchical technique proposed by Harjo *et al.* (2004) may be referred to.

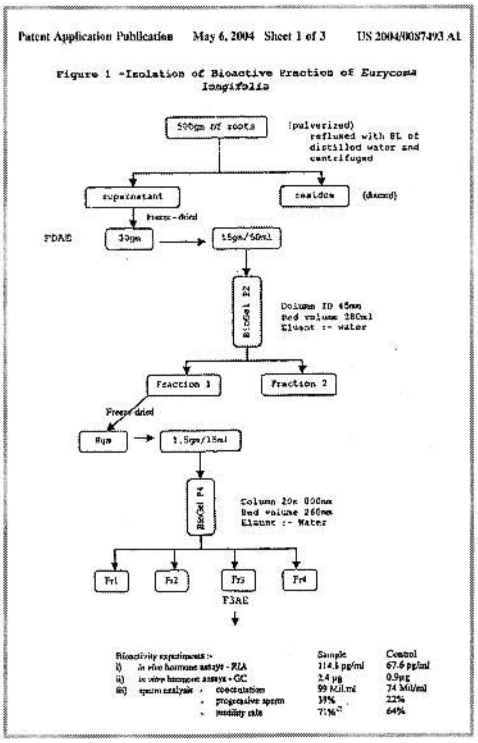

Figure 3: Biaoctive Tongkat Ali fraction process diagram (Sambandan et al. 2004)

PRODUCT DEVELOPMENT

A key area that Malaysia can differentiate itself from other herbal producers is in the development of knowledge based herbal products from local herbs. With the rich knowledge from Traditional Chinese Medicine (TCM), Indian Ayurveda and Malay medicine, products can be formulated that can give maximum wellness benefits. For instance, although individual herbs are powerful, it is the combination of the herb within the framework of this knowledge that can render it effective.

In TCM, herbs can be combined to give the correct mixture of the different energies and humours. One good example is the combination of Ginseng (*Panax ginseng*) and Lingzhi (*Ganoderma lucidum*) to form a powerful immune enhancer. Ayurvedic medicine, on the other hand, emphasises that the delivery of drugs should be within a specific time and form. Ayurvedic medicines are usually consumed in a raw liquid form as taste and freshness are important within the Ayurvedic context to ensure the efficacy of the herb. Therefore, the herb product should be closest to the raw form preferably a liquid or a paste rather than a tablet.

EXPERIENCE AT THE CEPP, UNIVERSITI TEKNOLOGI MALAYSIA

The Chemical Engineering Pilot Plant (CEPP) is a centre of excellence set up at Universiti Teknologi Malaysia by the Malaysian government. The main focus of CEPP in its research activities is on the area of process and product development based on local available natural products through phytochemical processing and bioprocess engineering. Among phytochemical related work at CEPP include the process development of Tongkat Ali spray dry extract, Turbo Extractor Distiller optimisation for essential oil production and a novel process design for multiple product processing.

Tongkat Ali extract powder is produced from water extracts of Tongkat Ali roots that have been spray dried as shown in Figure 2. When the process was first commercialised by a local herbal corporation, the extraction process consisted of a six hour atmospheric boiling operation which produced a relatively low product yield with high energy costs. After optimisation studies at CEPP, the industrial extraction process was shortened to 2 hours with a higher yield due to the higher extraction temperature of 110°C and higher extraction ratio. The energy costs were also reduced significantly. The process is currently being further optimised for standardisation based on the target compounds such as eurycomanone, the dominant quassinoid present in the extract.

The Turbo Extractor Distiller is a combination of a grinder, boiler, and distiller in a single device as shown in Figure 4. It is an ideal apparatus for producing a variety of products such as oleoresins, essential oils, and fragrance extracts. Raw material such as bark, leaves, and roots are simultaneously ground and boiled and the vapour is condensed into the desired products. The process optimisation of essential oil extraction has been performed using this integrated equipment.

The engineering issue addressed was to optimise the production of essential oils as a function of the raw material loading weight. To acquire optimal extraction there must be sufficient heat transfer between the heating surface and the raw material through the solvent. If the sample is too heavily loaded, the raw material will contact the heating surface directly and the heat transfer will be reduced leading to lower extraction. However, if the loading is too low, the energy transfer may not be sufficient due to the high volume of solvent. Figure 5 shows the optimal extraction loading weight found through optimisation studies at CEPP. An important point to note is that in optimisation for processes that combine mass and heat transfer may require optimisation studies such as these.

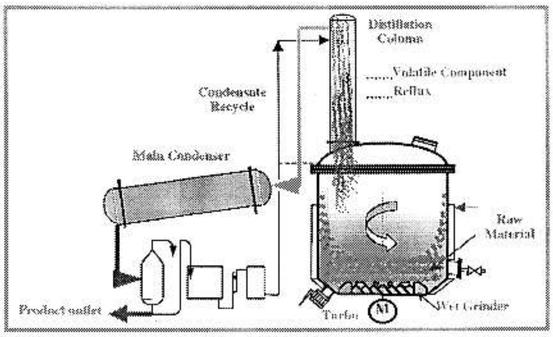

Figure 4: Turbo extractor distiller

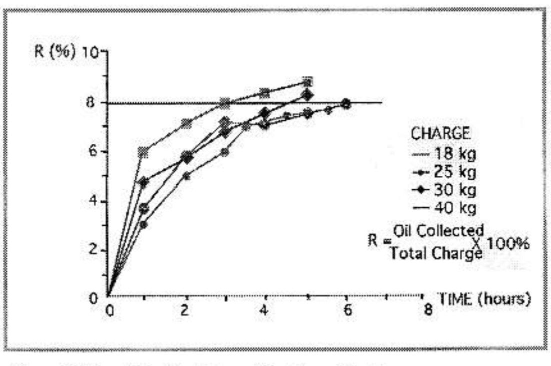

Figure 5: Essential oil yield as a function of loading

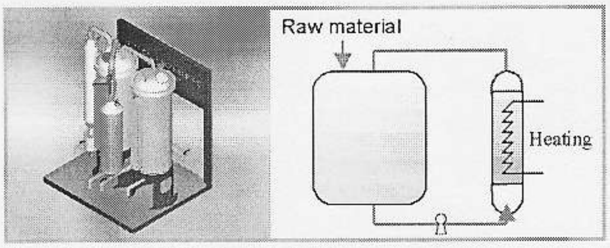

Figure 6: Integrated phytochemical extraction process

CEPP has also developed an integrated phytochemical extraction process as shown in Figure 5. This design consists of an extraction column, a condenser, a multipurpose extraction vessel, a filtration unit and a recirculation pump. Depending on the process setup as shown, different operations can be executed to produce whole plant extract, concentrated extract, purified extract, essential oils, concretes and oleoresins. This allows for local manufacturers to produce a wider variety of products with the same equipment, hence lowering capital costs.

CONCLUSION

Malaysia intends to become a key herbal medicine producer for global and local demands based on its abundant variety of herbs and strong knowledge base of its various races and indigenous groups. An important aspect of this aspiration is the engineering capacity to produce these products which require the application of process and product development to herbal processing. Currently, physical and chemical data is severely lacking in this field as well as an integrated process design methodology. It is important that more studies be undertaken in this area with the view of immediate application as the global market for herbal products is rapidly growing. ■

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